

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Carl Towns et al.)	For: Polymers, Their Preparation
)	and Uses
Serial No. 10/578,895)	
)	Group Art Unit: 1786
Filed: November 10, 2004 (Int'l.)	
Appl. No. PCT/GB2004/004754))	Examiner: Brett Alan Crouse
)	
)	Confirmation No. 3448

DECLARATION UNDER 37 C.F.R. § 1.132 OF ANDREW B. HOLMES, Ph.D.

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Andrew B. Holmes, Ph.D., hereby declare as follows:

1. As mentioned in the Declaration under 37 CFR § 1.132 of Andrew B. Holmes, Ph.D. filed April 8, 2011 (hereafter, “the previous Rule 132 Declaration”), I am a co-inventor of the subject matter claimed in the above-identified patent application (hereafter, “the patent application”). I am familiar with the patent application, the June 15, 2011 final action (hereafter, “the final action”), and the documents cited therein.

2. At p. 6, section 6 of the final action, the Examiner explained/asserted that:

Kreuder has been added to the rejection over Kobayashi to provide a showing that the public was in possession of the method of making dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant. The reference also teaches that the method taught by Kobayashi would successfully result in the production of dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant as taught by Kobayashi. Thus, Kobayashi provides an enabling disclosure to one of ordinary skill in the art.

3. As stated at p. 4, paragraph 11 of the previous Rule 132 Declaration:

The only worked examples reported in Kobayashi for converting compound F (5) into a dihalo-substituted dibenzosilole molecule include the subsequent halogenation of compound F (5) to produce compounds G (6) and H (pp.40-41, Synthetic Example 10) as illustrated by the general synthesis reaction below.



4. Thus, Kobayashi teaches the **aromatic electrophilic bromination** (i.e., substitution of Br^+ for H^+ on the aromatic ring) of an electron rich alkoxy-substituted dibenzosilole using N-bromosuccinimide as illustrated in paragraph 3 (above) and in paragraph 11 of the previous Rule 132 Declaration. The use of N-bromosuccinimide as a mild source of Br_2 (molecular bromine) in aromatic electrophilic brominations is well understood. See, for example, March, *Advanced Organic Chemistry: Reactions, Mechanisms and Structure*, 4th ed., John Wiley & Sons, New York, p. 532 (1992), which illustrates the bromination of a phenol using a reagent such as N-bromosuccinimide.¹

5. As detailed in paragraphs 12-14 of the previous Rule 132 Declaration, the electrophilic bromination reaction allegedly taught by Kobayashi is not enabling for a polymer comprising a dibenzosilole repeat unit having H or an electron withdrawing substituent at the 3- and 6- positions, as recited by formula (I) of claim 1 in the patent application because **halo-desilylation** occurs in the absence of any competing strong electron donating substituent. Thus, Kobayashi does not teach “the production of dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant” as asserted by the Examiner. See final action at pp. 6-7.

¹ Copy attached as Attachment A.

6. With respect to U.S. Patent No. 6,329,082 to Kreuder et al. (“Kreuder”), the Examiner referenced Example 7 in asserting that Kreuder evidences that Kobayashi has an enabled disclosure. *See* p. 4 of the final action. In Examples 6 and 7, 2,2'-dilithiobibenzyl is prepared by transmetallation of the corresponding 2,2'-dibromobibenzyl with n-butyl-lithium. Reaction of 2,2'-dilithiobibenzyl with silicon tetrachloride then affords bis(bibenzyl-2,2'-diyl)silane.² Bis(bibenzyl-2,2'-diyl)silane is then reacted with N-bromosuccinimide in carbon tetrachloride in the presence of a light source to obtain bis(α,α' (β')-dibromobibenzyl-2,2'-diyl)silane. The reactions are shown below:



7. The above reaction scheme demonstrates that Kreuder teaches **benzylic side chain halogenations** (i.e., introduction of a halogen reagent to replace a hydrogen atom on a carbon attached to an aromatic ring). Further, the reaction conditions of N-bromosuccinimide in carbon tetrachloride in the presence of a light source corroborate that Kreuder teaches benzylic side chain halogenation. *See*, for example, March, pp. 694, 695 (1992).³

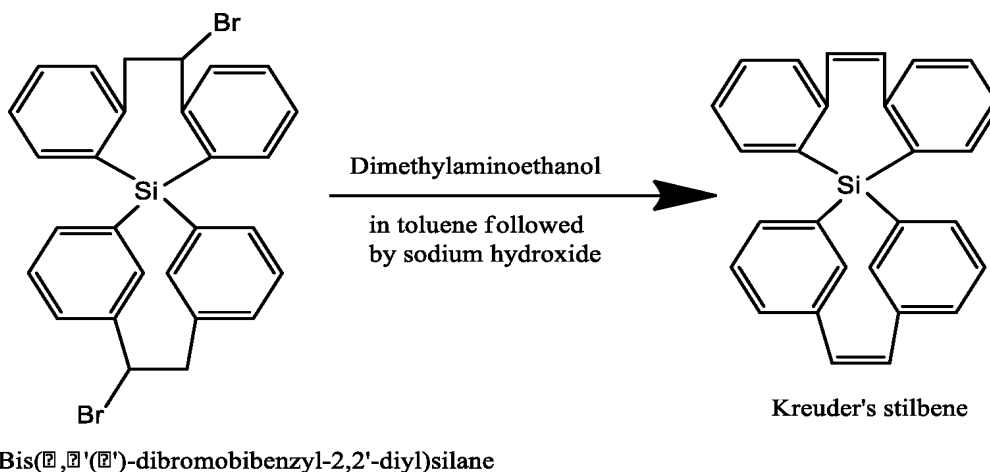
8. In this regard, March teaches that benzylic side chain halogenation is a species of “allylic halogenation.” For example, March teaches that “NBS is also a highly regioselective brominating agent at other positions including positions α to a carbonyl group, to a C \equiv C triple bond, and **to an aromatic ring (benzylic position).**” *Id.* at p. 695, lines 17-19. Specific reaction conditions are used in allylic halogenations, for example, “[a] non polar solvent is used, most often CCl₄.” *Id.* at p. 695, lines 1-2. Further, “[w]ith any reagent [such as N-bromosuccinimide] an initiator is needed; this is usually a peroxide or, less often, uv light.” *Id.* at p. 695,

² The structure illustrated at p. 4, section 4 of the final action as corresponding to bis(bibenzyl-2,2'-diyl)silane is incorrect. The correct structure is the middle structure in the scheme illustrated in paragraph 6, above.

³ Copy attached as Attachment A.

lines 4-5. Based on my expertise and experience, a 300W incandescent tungsten lamp as used in Kreuder is also a suitable initiator. Consistent with the foregoing, when discussing promoting aromatic electrophilic substitution, March teaches that “[s]ince side-chain halogenation is catalyzed by light, the reactions should be run in the absence of light wherever possible.” *Id.* at p. 532, lines 11-13. Finally, March discloses that “the mechanism of allylic bromination is of the free radical type....” *Id.* at p. 695, line 21.

9. In Kreuder Example 7, a combination of bis(bibenzyl-2,2'-diyl)silane and “N-bromosuccinimide in 100 ml of **tetrachloromethane** were heated to boiling **under irradiation** with a 300 W incandescent tungsten lamp.” One of ordinary skill in the art would recognize that these reaction conditions lead to benzylic halogenation as the reactive species is a bromine free radical (not molecular bromine) and thus to the right hand compound in the scheme illustrated in paragraph 6 where the bromine atoms are attached to benzylic carbon atoms in the bridging position and not to the aromatic ring. The bromine atoms must be on the bridging positions as the next stage described by Kreuder is a dehydrohalogenation reaction with diethylaminomethanol and then sodium hydroxide to afford the claimed stilbene (see below).



Thus, like Kobayashi, the combination of Kobayashi and Kreuder also does not teach “the method of making dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant” as asserted by the Examiner. *See* final action at p. 7.

10. At p. 7 of the final action, the Examiner explained/asserted that:

Kreuder has been added to the rejection over Roberts to provide a showing that the public was in possession of the method of making dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant.

11. As stated at pp.6-7, paragraph 18 of the previous Rule 132 Declaration:

...Roberts only teaches preparation of carbon bridged materials and provides no teachings regarding the synthesis of a polymer comprising a dibenzosilole repeat unit, much less a polymer comprising a dibenzosilole repeat unit having H or an electron withdrawing substituent at the 3- and 6- positions, as recited by formula (I) of claim 1 in the patent application. There is no disclosure in Roberts regarding how Si atoms are introduced into the dibenzosiloles shown as compounds XXXIV and LIV. Consequently, Roberts is not enabling for a polymer comprising a dibenzosilole repeat unit having H or an electron withdrawing substituent at the 3- and 6- positions, as recited by formula (I) of claim 1 in the patent application.

12. Kreuder does not remedy any of the previously noted deficiencies in Roberts. Thus, the combination of Roberts and Kreuder does not teach “the method of making dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant” as asserted by the Examiner. *See* final action at p. 7.

13. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the above-referenced patent application and any patent issued therefrom.

Date: September 14th, 2011

By

Andrew B. Holmes

Andrew B. Holmes, Ph.D.

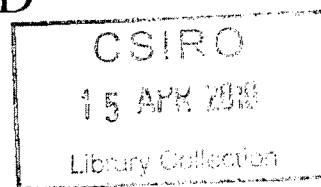
ORGANIC CHEMISTRY

REACTIONS,
MECHANISMS, AND
STRUCTURE

FOURTH EDITION

Jerry March

Professor of Chemistry
Adelphi University



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Library of Congress Cataloging in Publication Data:

March, Jerry, 1929—

Advanced organic chemistry : reactions, mechanisms, and structure
/ Jerry March. — 4th ed.
p. cm.

“A Wiley-Interscience publication.”

Includes bibliographical references and indexes.

ISBN 0-471-60180-2 (alk. paper)

1. Chemistry. Organic. I. Title.

QD251.2.M37 1992

547—dc20

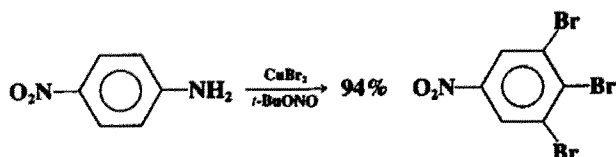
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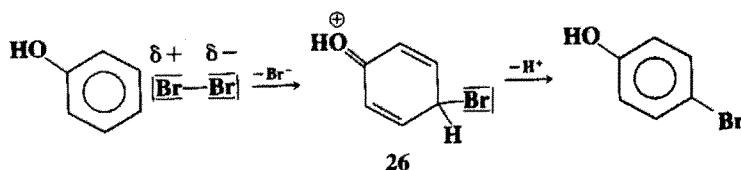
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to the OH_2^+ group, which should be meta-directing because of its positive charge. Bromination and the Sandmeyer reaction (4-25) can be carried out in one laboratory step by treatment of an aromatic primary amine with CuBr_2 and *t*-butyl nitrite, e.g.,¹⁸²



Other reagents have been used, among them HOCl ,¹⁸³ HOBr , and *N*-chloro and *N*-bromo amides (especially *N*-bromosuccinimide and tetraalkylammonium polyhalides¹⁸⁴). In all but the last of these cases the reaction is catalyzed by the addition of acids. Dibromoisocyanuric acid in H_2SO_4 is a very good brominating agent¹⁸⁵ for substrates with strongly deactivating substituents.¹⁸⁶ Two particularly powerful reagents consist of (1) S_2Cl_2 and AlCl_3 in sulfuryl chloride (SO_2Cl_2) (the *BMC reagent*)¹⁸⁷ and (2) dichlorine oxide Cl_2O and a strong acid such as sulfuric.¹⁸⁸ If the substrate contains alkyl groups, side-chain halogenation (4-1) is possible with most of the reagents mentioned, including chlorine and bromine. Since side-chain halogenation is catalyzed by light, the reactions should be run in the absence of light wherever possible.

For reactions in the absence of a catalyst, the attacking entity is simply Br_2 or Cl_2 that has been polarized by the ring.¹⁸⁹



Evidence for molecular chlorine or bromine as the attacking species in these cases is that acids, bases, and other ions, especially chloride ion, accelerate the rate about equally, though if chlorine dissociated into Cl^+ and Cl^- , the addition of chloride should decrease the rate and the addition of acids should increase it. The conjugate base of **26** (4-bromo-2,5-cyclohexadienone) has been detected spectrally in the aqueous bromination of phenol.¹⁹⁰

When a Lewis-acid catalyst is used with chlorine or bromine, the attacking entity may be Cl^+ or Br^+ , formed by $\text{FeCl}_3 + \text{Br}_2 \rightarrow \text{FeCl}_3\text{Br}^- + \text{Br}^+$, or it may be Cl_2 or Br_2 , polarized by the catalyst. With other reagents, the attacking entity in brominations may be Br^+ or a species such as H_2OBr^+ (the conjugate acid of HOBr), in which H_2O is a carrier of Br^+ .¹⁹¹

¹⁸²Doyle; Van Lente; Mowat; Fobare *J. Org. Chem.* **1980**, *45*, 2570.

¹⁸³For the use of calcium hypochlorite, see Nwaukwa; Keehn *Synth. Commun.* **1989**, *19*, 799.

¹⁸⁴See Kajigaeshi; Moriaki; Tanaka; Fujisaki; Kakinami; Okamoto *J. Chem. Soc., Perkin Trans. 1* **1990**, 897, and other papers in this series.

¹⁸⁵Nitrobenzene is pentabrominated in 1 min with this reagent in 15% oleum at room temperature.

¹⁸⁶Gottardi *Monatsh. Chem.* **1968**, *99*, 815, **1969**, *100*, 42.

¹⁸⁷Ballester; Molinet; Castañer *J. Am. Chem. Soc.* **1960**, *82*, 4254; Andrews, Glidewell; Walton *J. Chem. Res. (S)* **1978**, 294.

¹⁸⁸Marsh; Farnham; Sam; Smart *J. Am. Chem. Soc.* **1982**, *104*, 4680.

¹⁸⁹For reviews of the mechanism of halogenation, see de la Mare, Ref. 171; de la Mare; Swedlund, in Patai *The Chemistry of the Carbon-Halogen Bond*, pt. 1; Wiley: New York, 1973; pp. 490-536; Taylor, in Bamford; Tipper, Ref. 1, pp. 83-139; Berliner *J. Chem. Educ.* **1966**, *43*, 124-133. See also Schubert; Dial *J. Am. Chem. Soc.* **1975**, *97*, 3877; Keefer; Andrews *J. Am. Chem. Soc.* **1977**, *99*, 5693; Briggs; de la Mare; Hall *J. Chem. Soc., Perkin Trans. 2*

With HOCl in water the generally AcOCl . All these doubtful that Cl^+ is a significant demonstrated in the reaction chlorine attacking entity at ranges (as in 1-35) to give a isomer predominates.¹⁹³

FeCl_3 itself, and also Cu . The electrophile might be by a free-radical mechanism.

When chlorination or bromination ortho-para-directing groups here, which is not complete by the SEI mechanism, e.g. *zene*.¹⁹⁸

2. Iodine. Iodine is the for active substrates, an oxidizing electrophile.²⁰⁰ Examples of and H_2O_2 .²⁰¹ ICl is a better used have been IF (prepared from I_2 and FeCl_3), I_2 and FeCl_3 (which gives FeCl_4^- and I^+), and the combination of I_2 and $\text{CF}_3\text{SO}_3\text{Ag}$,²⁰⁸ $\text{HgO}-\text{BF}_3$,²⁰⁹ TlOAc method is regioselective.

The actual attacking species too unreactive, except for active

¹⁹²Swain; Crist *J. Am. Chem. Soc.*

¹⁹³Haberfeld; Paul *J. Am. Chem. Soc.*

Paul; Habersfeld *J. Org. Chem.* **1976**,

¹⁹⁴Kovacic; Wu; Stewart *J. Am. Chem. Soc.*

Commandeur; Mathais; Raynier; Wacziarg; *J. Org. Chem. USSR* **1988**, *24*, 211; K

¹⁹⁵For a review of halogenations with I_2 and H_2O_2 , see

¹⁹⁶Nonhebel *J. Chem. Soc.* **1963**, 1.

¹⁹⁷For a review of this type of reaction, see

¹⁹⁸Mach; Bunnett *J. Am. Chem. Soc.*

¹⁹⁹For reviews of I_2 as an electrophile, see

1977, pp. 227-276. For reviews of aromatic iodination, see

1984, *53*, 343-350.

²⁰⁰Butler *J. Chem. Educ.* **1971**, *48*,

²⁰¹For a discussion, see Makhon'ko; Kozlov; Chepurkov; Rodkin; Beletskii

²⁰²For a review of ICl , see McClelland; Rozen; Zamir *J. Org. Chem.* **1975**, *40*, 191.

²⁰³See Kajigaeshi; Kakinami; Watanabe; *J. Org. Chem.* **1978**, *43*, 2277.

²⁰⁴Radner *Acta Chem. Scand.* **1989**, *43*, 5287.

²⁰⁵Baird; Surridge *J. Org. Chem.* **1971**, *36*, 1800.

²⁰⁶khon'kov; Chepurkov; Rodkin; Beletskii; Uemura; Onoe; Okano *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1000.

²⁰⁷Kobayashi; Kumadaki; Yoshida *J. Org. Chem.* **1980**, *45*, 486.

²⁰⁸Koveshnikova *Synthesis* **1980**, 486.

²⁰⁹Barluenga; Campos; González *J. Org. Chem.* **1980**, *45*, 486.

TABLE 14.4 Some *D* values¹⁰⁶

Bond	<i>D</i>	
	kcal/mol	kJ/mol
H-F	136	570
H-Cl	103	432
H-Br	88	366
H-I	71	298
F-F	38	159
Cl-Cl	59	243
Br-Br	46	193
I-I	36	151
CH ₃ -F	108	452
CH ₃ -Cl	85	356
CH ₃ -Br	70	293
CH ₃ -I	57	238

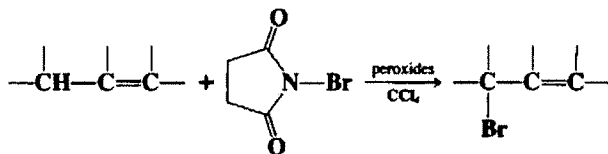
to be $F_2 > Cl_2 > Br_2 > I_2$ is the decreasing strength of the HX bond in the order $HF > HCl > HBr > HI$. The increased reactivity of secondary and tertiary positions is in accord with the decrease in *D* values for R—H in the order primary > secondary > tertiary (Table 5.3). (Note that for chlorination step 1 is exothermic for practically all substrates other than CH_4 , since most other aliphatic C—H bonds are weaker than those in CH_4 .)

Bromination and chlorination of alkanes and cycloalkanes can also take place by an electrophilic mechanism if the reaction is catalyzed by $AgSbF_6$.¹¹² Direct chlorination at a vinylic position by an electrophilic mechanism has been achieved with benzeneseleninyl chloride $PhSe(O)Cl$ and $AlCl_3$ or $AlBr_3$.¹¹³ However, while some substituted alkenes give high yields of chloro substitution products, others (such as styrene) undergo addition of Cl_2 to the double bond (5-26).¹¹³ Electrophilic fluorination has already been mentioned (p. 690).

OS II, 89, 133, 443, 549; III, 737, 788; IV, 807, 921, 984; V, 145, 221, 328, 504, 635, 825; VI, 271, 404, 715; VII, 491; 65, 68.

4-2 Allylic Halogenation

Halogenation or Halo-de-hydrogenation



This reaction is a special case of 4-1, but is important enough to be treated separately.¹¹⁴ Olefins can be halogenated in the allylic position by a number of reagents, of which N-bromosuccinimide (NBS)¹¹⁵ is by far the most common. When this reagent is used, the

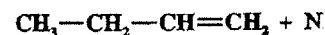
¹¹²Olah; Renner; Schilling; *Mo J. Am. Chem. Soc.* 1973, 95, 7686. See also Olah; Wu; Farooq *J. Org. Chem.* 1989, 54, 1463.

¹¹³Comins; Sato; Yoshida *Bull. Chem. Soc. Jpn.* 1988, 61, 110.

REACTION 4-2

reaction is known as *Wohl-Z* CCl_4 . Other N-bromo amides nation has been carried out, sulfonamide,¹¹⁶ or *t*-butyl hyp usually a peroxide or, less oft

The reaction is usually quit However, when the allylic radi take place, so that mixtures o



When a double bond has tw secondary position is substitu tertiary hydrogen is not clear been performed.¹¹⁸ It is possit the electron-withdrawing natu side of the double bond rathe

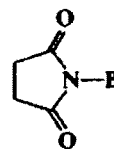
NBS is also a highly regio: sitions α to a carbonyl group position). When both a doubl position is α to the triple bon

That the mechanism of all: by Dauben and McCoy,¹²¹ w initiators and inhibitors and in is present. Subsequent work in the substrate is the bromine a it is formed, the main propag

Step 1

Step 2

The source of the Br_2 is a 1 step 1:



The function of the NBS is concentration and to use up

¹¹⁶Theilacker; Wessel *Liebigs Ann.*

¹¹⁷Walling; Thaler *J. Am. Chem. Soc.*

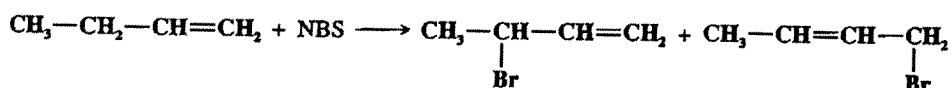
¹¹⁸Dauben; McCoy *J. Org. Chem.*

¹¹⁹Ucciani; Naudet *Bull. Soc. Chim.*

¹²⁰Peiffer *Bull. Soc. Chim. Fr.* 19

reaction is known as *Wohl-Ziegler bromination*. A nonpolar solvent is used, most often CCl_4 . Other N-bromo amides have also been used. To a much lesser extent, allylic chlorination has been carried out, with N-chlorosuccinimide, N-chloro-N-cyclohexylbenzenesulfonamide,¹¹⁶ or *t*-butyl hypochlorite.¹¹⁷ With any reagent an initiator is needed; this is usually a peroxide or, less often, uv light.

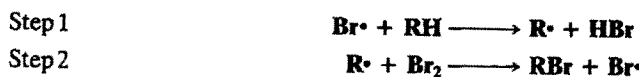
The reaction is usually quite specific at the allylic position and good yields are obtained. However, when the allylic radical intermediate is unsymmetrical, allylic rearrangements can take place, so that mixtures of both possible products are obtained, e.g.,



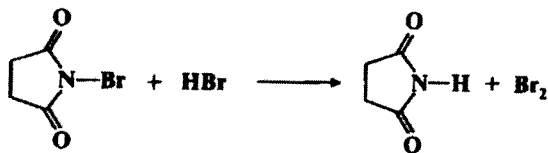
When a double bond has two different allylic positions, e.g., $\text{CH}_3\text{CH}=\text{CHCH}_2\text{CH}_3$, a secondary position is substituted more readily than a primary. The relative reactivity of tertiary hydrogen is not clear, though many substitutions at allylic tertiary positions have been performed.¹¹⁸ It is possible to brominate both sides of the double bond.¹¹⁹ Because of the electron-withdrawing nature of bromine, the second bromine substitutes on the other side of the double bond rather than α to the first bromine.

NBS is also a highly regioselective brominating agent at other positions, including positions α to a carbonyl group, to a $\text{C}\equiv\text{C}$ triple bond, and to an aromatic ring (benzylic position). When both a double and a triple bond are in the same molecule, the preferred position is α to the triple bond.¹²⁰

That the mechanism of allylic bromination is of the free-radical type was demonstrated by Dauben and McCoy,¹²¹ who showed that the reaction is very sensitive to free-radical initiators and inhibitors and indeed does not proceed at all unless at least a trace of initiator is present. Subsequent work indicated that the species that actually abstracts hydrogen from the substrate is the bromine atom. The reaction is initiated by small amounts of Br^\bullet . Once it is formed, the main propagation steps are



The source of the Br_2 is a fast ionic reaction between NBS and the HBr liberated in step 1:



The function of the NBS is therefore to provide a source of Br_2 in a low, steady-state concentration and to use up the HBr liberated in step 1.¹²² The main evidence for this

¹¹⁶Theilacker; Wessel *Liebigs Ann. Chem.* 1967, 703, 34.

¹¹⁷Walling; Thaler *J. Am. Chem. Soc.* 1961, 83, 3877.

¹¹⁸Dauben; McCoy *J. Org. Chem.* 1959, 24, 1577.

¹¹⁹Ucciani; Naudet *Bull. Soc. Chim. Fr.* 1962, 871.

¹²⁰Peiffer *Bull. Soc. Chim. Fr.* 1963, 537.